IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Colpitts et al.

Serial No.: 09/549,342

Filed: April 13, 2000

For: REAGENTS AND METHODS USEFUL FOR DETECTING DISEASES OF THE REPRODUCTIVE TISSUES

Attorney Docket No.: 5972.US.P6

Examiner: Harris, A.

Group Art Unit: 1642

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APPEAL BRIEF

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

This is an Appeal from the final rejection, dated April 22, 2002, of claims 1-6, 39 and 41-47. No claims stand allowed.

REAL PARTY IN INTEREST

All rights have been assigned to the inventors' employer (i.e., Abbott Laboratories) via recorded Assignment.

RELATED APPEALS AND INTERFERENCES

None exist to the knowledge of Applicant's attorney.

STATUS OF CLAIMS

Claims 1-6, 39 and 41-47 are pending in the application. The rejection of claims 1-6, 39 and 41-47 is appealed. The appealed claims are set forth in the Appendix.

STATUS OF AMENDMENTS/RESPONSES

A Response to Final Action was filed on July 22, 2002 in response to the final rejection dated April 22, 2002. (A Notice

of Appeal was filed on July 22, 2002.) An Advisory Action was mailed on September 30, 2002 indicating that the request for reconsideration was considered but did not place the application in condition for allowance. A telephonic interview was held with Examiner Harris on October 22, 2002 but did not result in allowance.

SUMMARY OF THE INVENTION

The present invention relates to a purified multimeric polypeptide antigen (MPA). In particular, the antigen comprises at least one EU250 polypeptide and at least one polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide. The antigen has a molecular weight of about 20-70 kilodaltons, an isoelectric point of about less than 8, and may further comprise at least one unknown polypeptide. The antigen may be utilized for many purposes. For example, the antigen may be used in the detection and diagnosis of uterine cancer, a potentially fatal disease which affects about 35,000 women a year.

ISSUES

The issue on appeal is as follows:

1) The Examiner has rejected claims 1-6, 39 and 41-47 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,066,724 (Ni et al.).

ISSUE 1

As a basis for the Section 103 rejection, the Examiner alleges that the sequences claimed are 100% homologous to the sequences taught in Ni et al., and that the sequences may be comprised within a larger polypeptide as well as combined.

GROUPING OF CLAIMS

The appellants submit that the rejected claims are independently patentable and do not stand or fall together.

Claim 1 refers to a purified multimeric polypeptide antigen (MPA) comprising at least one EU250 polypeptide (SEQ ID NO:3) and at least one polypeptide selected from the group consisting of a

BU101 polypeptide (SEQ ID NO:2) and a TU104 polypeptide (SEQ ID NO:10). Claim 2 recites that the antigen of claim 1 further comprises at least one unknown polypeptide. Claim 3 recites that the antigen of claim 1 has a molecular weight of about 20 to 70 kilodaltons. Claim 4 recites that the antigen of claim 3 has an isoelectric point less than 8, and claim 5 recites that the BU101 polypeptide (SEQUENCE ID NO:2) of the antigen of claims 1 or 2 contains a polymorphism at amino acid position number 53 selected from the group consisting of proline and leucine.

Claim 39 refers to a composition of matter comprising a multimeric polypeptide antigen, wherein the antigen comprises at least one EU250 polypeptide and at least one polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide. Claim 41 refers to the composition of matter of claim 39 wherein the composition further comprises at least one antibody, bound to the multimeric polypeptide antigen, wherein the antibody is specific to at least one polypeptide selected from the group consisting of a EU250 polypeptide, a BU101 polypeptide, a TU104 polypeptide and a polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10. Claim 42 refers to the composition of matter of claim 41 wherein two antibodies are present and each binds to a separate polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10. Claim 43 refers to the composition of matter of claim 42 wherein each of the two antibodies binds to a EU250 polypeptide. Claim 44 refers to the composition of matter of claim 42 wherein each of the two antibodies binds to a polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide. Claim 45 refers to the composition of matter of claim 42 wherein one of the two antibodies binds to a EU250 polypeptide and the other of the two antibodies binds to a polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide. Claim 46 refers to the composition of matter of claim 42 wherein one of the two antibodies binds to a EU250 polypeptide and the other of the two antibodies binds to a

polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10. Claim 47 refers to the composition of matter of claim 42 wherein one of the two antibodies binds to a polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide, and the other of the two antibodies binds to a polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10.

APPELLANTS' ARGUMENTS

The appellants submit that the pending claims are all patentable over the Ni et al. reference cited above.

ISSUE 1

The Prior Art Rejection

The Examiner has rejected claims 1-6, 39 and 41-47 under Section 103 as being unpatentable over U.S. Patent No. 6,066,724 (Ni et al.). In particular, on page 8 of the Office Action of September 17, 2001 (i.e., Paper No. 10), the Examiner states that ``it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the polypeptides, variants, fragments and other compounds of the patent, such as antibodies, pharmaceutical carriers of homologs.''

In the final rejection of April 22, 2002 (Paper No. 13), the Examiner contends that appellants' claimed sequences SEQ ID NO:2 (BU101) and 3 (EU250) are 100% homologous to sequences hESF II and III, respectively, of U.S. Patent No. 6,066,724. Further, the Examiner contends that col. 16, lines 21-24 of U.S. Patent No. 6,066,724 clearly state that the sequences referred to therein, as well as hESF I which is 92.4% homologous to appellants' SEQ ID:10 (TU104), are comprised within a larger polypeptide. Also, the Examiner alleges that the patent teaches the combination of the sequences, as well as polyclonal or monoclonal antibodies produced by the use of the polypeptide sequences. In summary, in the final rejection, the Examiner

asserts that, due to the above reasons, as well as those presented in Paper No. 10, the Section 103 rejection is maintained.

In contrast to the Examiner's contentions, the appellants assert that U.S. Patent No. 6,066,724 teaches hESF I, II and III polypeptides and uses thereof; however, there is absolutely no disclosure or suggestion in the patent as to the use of the polypeptides in combination and making up part of a complex or a multimeric polypeptide antigen (see independent claims 1 and 39 of the Appendix). More specifically, in col. 5, lines 13-17 of U.S. Patent No. `724, the statement is made that ``there are provided compositions comprising a hESF I, II or III polynucleotide or a hESF I, II or III polypeptide for administration to cells in vitro, to cells ex vivo and to cells in vivo, or to a multicellular organism.'' Thus, the ``or'' language clearly indicates that the hESF sequences described in the cited patent are used alone and not in combination. The patent does not use ``and/or'' language or ``and'' language when referring to the compositions.

Also, in col. 29, lines 25-34 of the patent, the following statement is made:

> The invention also relates to compositions comprising the polynucleotide or the polypeptides discussed above or the agonists or antagonists. Thus, the polypeptides of the present invention may be employed in combination with a non-sterile or sterile carrier for use with cells, tissues or organisms, such as a pharmaceutical carrier suitable for administration to a subject. Such compositions comprise, for example, a media additive or a therapeutically effective amount of **a polypeptide** of the invention and a pharmaceutically acceptable carrier or excipient. [emphasis added]

Once again, the ``a polypeptide'' language of the patent indicates that hESF I, II or III is used alone in the composition. Thus, this language provide further support for the concept that the polypeptides of the patent are never present in combination in the composition, unlike in the present invention.

In particular, there is absolutely no disclosure or suggestion in the cited reference that the sequence corresponding to EU250 (i.e., hESF III) of the claimed invention must be present in a multimeric polypeptide antigen or complex, as in the claimed invention. Thus, one of ordinary skill in the art certainly would not have been motivated to have used this particular sequence (i.e., EU250) in combination with BU101 and/or TU104 (and possibly at least one other polypeptide) based upon the teachings and suggestions of U.S. Patent No. 6,066,724, nor would one of ordinary skill in the art have been motivated to have developed an antibody against the combination or complex (see claims 41-47 of the Appendix).

Furthermore, it should also be noted that the Examiner states that the TU104 sequence of the present invention (see, e.g., claim 1 of the Appendix) is 92.4% similar to the sequence of U.S. Patent No. 6,066,724. Due to the lack of 100% similarity between amino acid sequences, it would appear to be inappropriate for the Examiner to compare TU104 (SEQ ID NO:10) to the hESF III sequence of the patent. In particular, such amino acid sequence differences support the concept that the present invention is not obvious over the patent.

Additionally, appellants submit that U.S. Patent No. 6,066,724 discloses that fragments of the polypeptides disclosed therein may be part of a larger molecule (see col. 16, lines 13-16). However, such fragments are not claimed in the present application. Only the full-length polypeptides are claimed (see claim 1 of the Appendix). In fact, U.S. Patent No. `724 defines a ``fragment'' as ``a polypeptide having an amino acid sequence that entirely is the same as part but not all of the amino acid sequence of ▒ hESFI, II and III polypeptides and variants or derivatives thereof.'' (See col. 16, lines 13-16.) Thus, the ``larger molecule'' of U.S. Patent No. `724 cannot contain the full-length amino acid sequences or polypeptides of the present invention, in combination, by distinct definition. This ``larger molecule'' may contain only fragments of the sequences disclosed in the patent.

Additionally, in col. 16, lines 17-33 of U.S. Patent No. 6,066,727, the following statements are made:

> Such fragments may be ''free-standing,'' i.e., not part of or fused to other amino acids or polypeptides, or they may be comprised within a larger polypeptide of which they form a part or region. When comprised within a larger polypeptide, the presently discussed fragments most preferably form a single contiguous region. However, several fragments may be comprised within a single larger polypeptide. For instance, certain preferred embodiments relate to a fragment of a hESF I, II or III polypeptide of the present [sic] comprised within a precursor polypeptide designed for expression in a host and having heterologous pre and propolypeptide regions fused to the amino terminus of the hESF I, II and III fragment and an additional region fused to the carboxyl terminus of the fragment. Therefore, fragments in one aspect of the meaning intended herein, refers to the portion or portions of a fusion polypeptide or fusion protein derived from hESF I, II and III.

Again, this language supports the concept that hESF I, II and III fragments are not used in combination in creating a complex. Rather, they may form a single contiguous region or may be part of a single polypeptide. Also, as stressed above, such fragments do not, by definition, represent the full-length amino acid sequences of hESF I, II or III. As stated above, in the present invention, only full-length polypeptide sequences are claimed.

In view of the above, it is submitted that the teachings and suggestions of U.S. Patent No. `724 would not have motivated one of ordinary skill in the art to have created the claimed invention at the time the application was filed, and that the Section 103 rejection should therefore be withdrawn. In particular, one of ordinary skill in the art would not have been motivated to have utilized the full-length polypeptide sequences of the claimed invention, in combination, based upon the disclosure or suggestions of U.S. Patent No. 6,066,724. Thus, appellants submit that the claimed invention is not rendered

obvious over U.S. Patent No. 6,066,724 and is therefore fully patentable.

In conclusion, the appellants submit that the Examiner's rejection should be reversed, and that the pending claims should be allowed.

Respectfully submitted,
Colpitts, et al.

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APPENDIX

The claims on Appeal are as follows:

1. A purified multimeric polypeptide antigen (MPA) comprising at least one EU250 polypeptide (SEQ ID NO:3) and at least one polypeptide selected from the group consisting of a BU101 polypeptide (SEQ ID NO:2) and a TU104 polypeptide (SEQ ID NO:10).

2. The antigen of claim 1 wherein said antigen further comprises at least one unknown polypeptide.

3. The antigen of claim 1 wherein said antigen has a molecular weight of about 20 to 70 daltons.

4. The antigen of claim 4 wherein said antigen has an isoelectric point of about less than 8.

5. The antigen of claims 1 or 2 wherein said at least one BU101 polypeptide (SEQUENCE ID NO:2) contains a polymorphism at amino acid position number 53 selected from the group consisting of proline and leucine.

6. The antigen of claims 1 or 2 wherein said at least one EU250 polypeptide and said at least one polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide are covalently linked by disulfide bonds.

39. A composition of matter comprising a multimeric polypeptide antigen, wherein said antigen comprises at least one EU250 polypeptide and at least one polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide.

41. The composition of matter of claim 39 wherein said composition further comprises at least one antibody, bound to said multimeric polypeptide antigen, wherein said antibody is specific to at least one polypeptide selected from the group

consisting of a EU250 polypeptide, a BU101 polypeptide, a TU104 polypeptide, a polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10.

42. The composition of matter of claim 41 wherein two antibodies are present and each binds to a separate polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10.

43. The composition of matter of claim 42 wherein each of said two antibodies binds to a EU250 polypeptide.

44. The composition of matter of claim 42 wherein each of said two antibodies binds to a polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide.

45. The composition of matter of claim 42 wherein one of said two antibodies binds to a EU250 polypeptide and the other of said two antibodies binds to a polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide.

46. The composition of matter of claim 42 wherein one of said two antibodies binds to a EU250 polypeptide and the other of said two antibodies binds to a polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10.

47. The composition of matter of claim 42 wherein one of said two antibodies binds to a polypeptide selected from the group consisting of a BU101 polypeptide and a TU104 polypeptide, and the other of said two antibodies binds to a polypeptide having an amino acid sequence selected from the group consisting of SEQUENCE ID NO:3, SEQUENCE ID NO:2 and SEQUENCE ID NO:10.